

FIGURE 1: SEQUENCE OF CDRS OF MOUSE MONOCLONAL 5/44

H1	NYWIH	(SEQ ID NO:1)
H2	GINPGNNYTTYKRNLKG	(SEQ ID NO:2)
H3	EGYGNYGAWFAY	(SEQ ID NO:3)
L1	RSSQSLANSYGNFLS	(SEQ ID NO:4)
L2	GISNRFS	(SEQ ID NO:5)
L3	LQGTHQPYT	(SEQ ID NO:6)

FIGURE 2: DNA/PROTEIN SEQUENCE OF 5/44 V_L

10	20	30	40	50															
GAT	GTT	GTG	ACT	CAA	ACT	CCA	CTC	TCC	CTG	CCT	GTC	AGC	TTT	GGA	GAT	CAA	GTT		
CTA	CAA	CAC	CAC	TGA	GTT	TGA	GGT	GAG	AGG	GAC	GGA	CAG	TCG	AAA	CCT	CTA	GTT	CAA	
D	V	V	V	T	Q	T	P	L	S	L	P	V	S	F	G	D	Q	V>	
60		70		80		90		100		110									
TCT	ATC	TCT	TGC	AGG	TCT	AGT	CAG	AGT	CTT	GCA	AAC	AGT	TAT	GGG	AAC	ACC	TTT	TTG	
AGA	TAG	AGA	AGA	ACG	TCC	AGA	TCA	GTC	TCA	GAA	CGT	TTG	TCA	ATA	CCC	TTG	TGG	AAA	AAC
S	I	S	C	R	S	S	Q	S	L	A	N	S	Y	G	N	T	F	L>	
120		130		140		150		160		170									
TCT	TGG	TAC	CTG	CAC	AAG	CCT	GGC	CAG	TCT	CCA	CAG	CTC	CTC	ATC	TAT	GGG	ATT	TCC	
AGA	ACC	ATG	GAC	GTG	TTC	GGG	CCG	GTC	AGA	GGT	GTC	GAG	GAG	TAG	ATA	CCC	TAA	AGG	
S	W	Y	L	H	K	P	G	Q	S	P	Q	L	L	I	Y	G	I	S>	
180		190		200		210		220											
AAC	AGA	TTT	TCT	GGG	GTG	CCA	GAC	AGG	TTC	ACT	GGC	AGT	GGT	TCA	GGG	ACA	GAT	TTC	
TTG	TCT	AAA	AGA	CCC	CAC	GGT	CTG	TCC	AAG	TGA	CCG	TCA	CCA	AGT	CCC	TGT	CTA	AAG	
N	R	F	S	G	V	P	D	R	F	T	G	S	G	S	G	T	D	F>	
230		240		250		260		270		280									
ACA	CTC	AAG	ATC	AGC	ACA	ATA	AAG	CCT	GAG	GAC	TTG	GGA	ATG	TAT	TAC	TGC	TTA	CAA	
TGT	GAG	TTC	TAG	TCG	TGT	TAT	TTC	GGG	CTC	CTG	AAC	CCT	TAC	ATA	ATG	ACG	AAT	GTT	
T	L	K	I	S	T	I	K	P	E	D	L	G	M	Y	Y	C	L	Q>	
290		300		310		320		330											
GGT	ACA	CAT	CAG	CCG	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG	CTG	GAA	ATA	AAA	CGT		
CCA	TGT	GTA	GTC	GGC	ATG	TGC	AAG	CCT	CCC	CCC	TGG	TTC	GAC	CTT	TAT	TTT	GCA		
G	T	H	Q	P	Y	T	F	G	G	G	T	K	L	E	I	K	R>		

FIGURE 3: DNA/PROTEIN SEQUENCE OF 5/44 V_H

10	20	30	40	50	
GAG GTC CAA CTG CAG CAG TCT GGG ACT GTA CTG GCA AGG CCT GGG GCT TCC GTG AAG					
CTC CAG GTT GAC GTC GTC AGA CCC TGA CAT GAC CGT TCC GGA CCC CGA AGG CAC TTC					
E V Q L Q Q S G T V L A R P G A S V K>					
60	70	80	90	100	110
ATG TCC TGC AAG GCT TCT GGC TAC AGG TTT ACC AAC TAC TGG ATT CAC TGG GTA AAA					
TAC AGG ACG TTC CGA AGA CCG ATG TCC AAA TGG TTG ATG ACC TAA GTG ACC CAT TTT					
M S C K A S G Y R F T N Y W I H W V V K>					
120	130	140	150	160	170
CAG AGG CCT GGG CAG GGT CTA GAA TGG ATT GGT GGT ATT AAT CCT GGA AAT AAT TAT					
GTC TCC GGA CCC GTC CCA GAT CTT ACC TAA CCA CCA TAA TTA GGA CCT TTA TTA ATA					
Q R P G Q G L E W I G G I N P G N N Y>					
180	190	200	210	220	
ACT ACG TAT AAG AGG AAC TTG AAG GGC AAG GCC ACA CTG ACT GCA GTC ACA TCC GCC					
TGA TGC ATA TTC TCC TTG AAC TTC CCG TTC CGG TGT GAC TGA CGT CAG TGT AGG CGG					
T T Y K R N L K G K A T L T A V T S A>					
230	240	250	260	270	280
AGC ACT GCC TAC ATG GAC CTC AGC AGC CTG ACA AGT GAG GAC TCT GCG GTC TAT TAC					
TCG TGA CGG ATG TAC CTC CTG GAG TCG TCG GAC TGT TCA CTC CTG AGA CGC CAG ATA ATG					
S T A Y M D L S S L T S E D S A V Y Y>					
290	300	310	320	330	340
TGT ACA AGA GAG GGC TAT GGT AAC TAC GGG GCC TGG TTT GCT TAC TGG GGC CAG GGG					
ACA TGT TCT CTC CCG ATA CCA TTG ATG CCC CGG ACC AAA CGA ATG ACC CCG GTC CCC					
C T R E G Y G N Y G A W F A Y W G Q G>					
350	360				
ACT CTG GTC ACC GTC TCC TCA					
TGA GAC CAG TGG CAG AGG AGT					
T L V T V S S>					

FIGURE 4: REMOVAL OF GLYCOSYLATION SITE AND REACTIVE LYSINE: PCR STRATEGY TO MUTATE CDR-H2 IN CH VECTOR

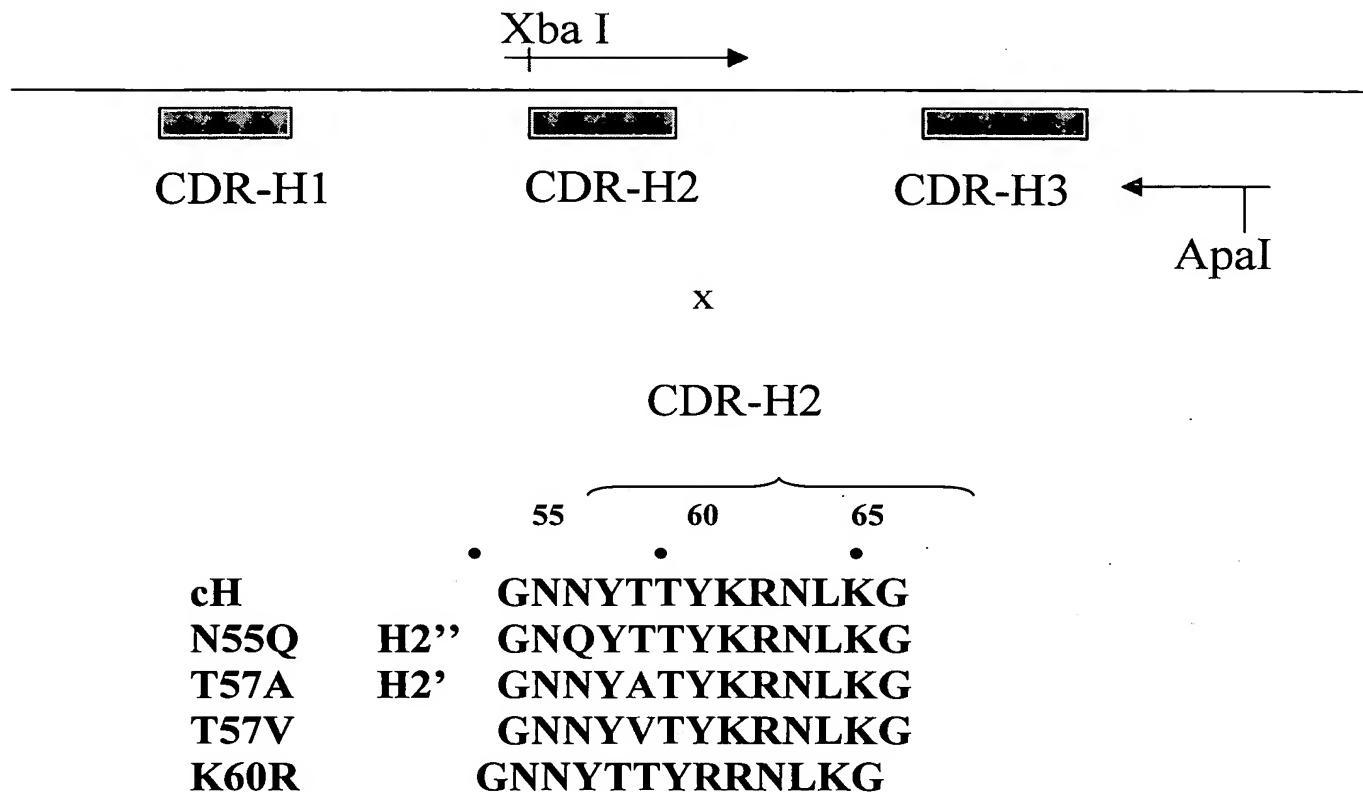


FIGURE 5: 5/44 LIGHT CHAIN SEQUENCE GRAFT DESIGN

	10	20		40
V _L	DVVVTQTPISLPVSFGDQVSISC	RSSQSLANSYGNFLS	WYLHKPGQSPQLLIY	
DPK9	DIQMTQSPSSLSASVGDRVITIC		WYQQKPGKAPKLLIY	
gL1	DVQVTQSPSSLSASVGDRVITIC	RSSQSLANSYGNFLS	WYLHKPGKA <u>Q</u> LLIY	
gL2	<u>DV</u> VVTQSPSSLSASVGDRVITIC	RSSQSLANSYGNFLS	WY <u>L</u> HKPGKA <u>Q</u> LLIY	
	60	70	80	90
V _L	GISNRFS GVPDRFTGSGSGTDFTLKISTIKPEDLGMYYC		LQGTHQPYT	
DPK9	GVPSRFSGSGSGTDFTLTISLQPEDFATYYC			
gL1	GISNRFS GVP <u>D</u> RFSGSGSGTDFTLTISLQPEDFATYYC		LQGTHQPYT	
gL2	GISNRFS GVP <u>D</u> RFSGSGSGTDFTLTISLQPEDFATYYC		LQGTHQPYT	
	100			
V _L	FGGGTKLEIKR			
JK1	FGQGTKVEIKR			
gL1	FGQGTKVEIKR			
gL2	FGQGTKVEIKR			

FIGURE 6: 5/44 HEAVY CHAIN SEQUENCE GRAFT DESIGN

	10	20	30	40	50	
V _H	EVQLQQSGTVLARP GASVKM SCKASGYRFT		NYWIH	WVKQRP GQGLEWIG	GINP	
DP7	QVQLVQSGAEVKKPGASVKVSCKASGYTFT			WVRQAPGQGLEWMG		
gH1	EVQLVQSGAEVKKPGASVKVSCKASGYRFT		NYWIH	WVRQAPGQGLEWIG	GINP	
gH4,5,6,7	EVQLVQSGAEVKKPGASVKVSCKASGYRFT		NYWIH	WVRQAPGQGLEWIG	GINP	
	60	70	80	90	100	
V _H	GNNYTTYKRN LKG	KATLTAVTSASTAYMDLSSLTSEDSAVYYCTR		EGYGN YG		
DP7	KFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCAR					
gH1	GNQYTTYKRN LKG	RATLTADTSTSTVYMELSSLRSEDTAVYYCTR		EGYGN YG		
gH4	GNNYATYRRN LKG	RATLTADTSTSTVYMELSSLRSEDTAVYYCTR		EGYGN YG		
gH5	GNNYATYRRN LKG	RVTMTADTSTSTVYMELSSLRSEDTAVYYCTR		EGYGN YG		
gH6	GNNYATYRRKF QG	RATLTADTSTSTVYMELSSLRSEDTAVYYCTR		EGYGN YG		
gH7	GNNYATYRRKF QG	RVTMTADTSTSTVYMELSSLRSEDTAVYYCTR		EGYGN YG		
	110					
JH4	WGQGTLTVSS					
V _H	AWFAY	WGQGTLTVSS				
gH1	AWFAY	WGQGTLTVSS				
gH4,5,6,7	AWFAY	WGQGTLTVSS				

FIGURE 7: MAP OF VECTOR PMRR14.

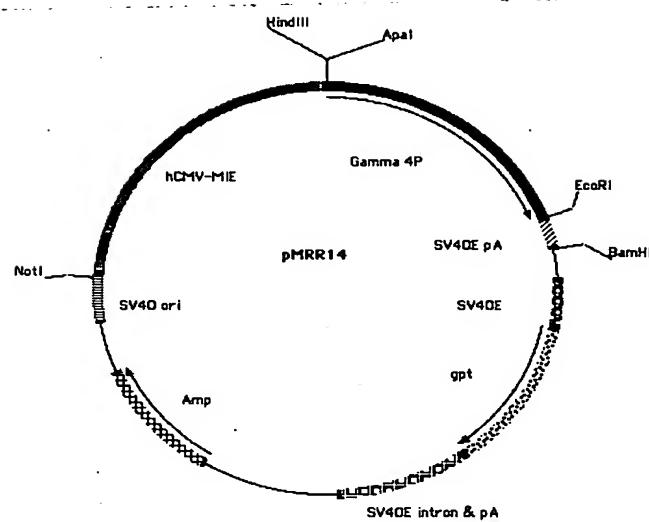


FIGURE 8: MAP OF VECTOR PMRR10.1

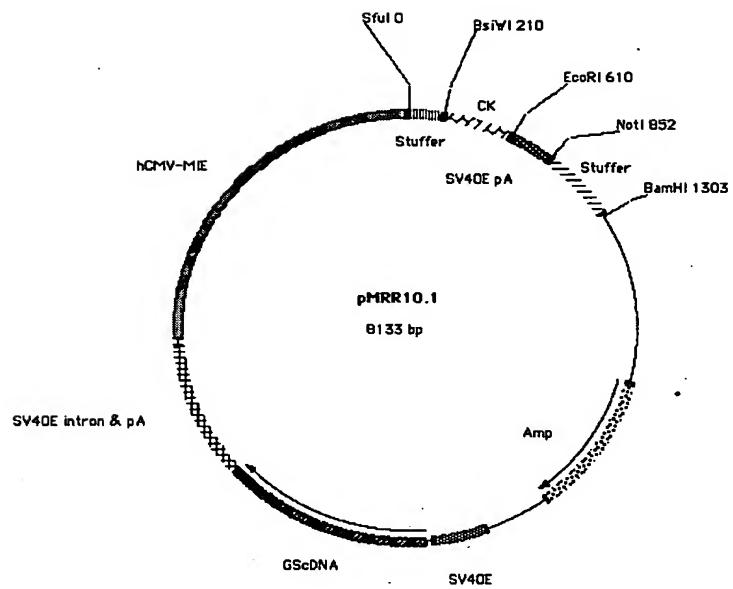


FIGURE 9: BIACORE ASSAY OF CHIMERIC 5/44 AND MUTANTS

	5/44	K_a e⁵	K_d e⁻⁴	KD e⁻¹⁰	~KD nM
	<u>cLcH</u>	2.9	1.14	3.93	0.4
	N55Q	5.81	1.9	3.27	0.3
	T57A	7.8	0.51	0.66	0.07
	K60R	4.95	1.01	2.04	0.2

FIGURE 10: OLIGONUCLEOTIDES FOR 5/44 GH1 AND GL1 GENE ASSEMBLIES

Heavy Chain

544gH1 T1

AGTGTGAGGTGCAATTGGTCCAGTCAGGAGCAGAGGTTAAGAACGCCTGGTCTCCGTC
AAAGTTCTGTAAAGGCTAGCGGCTACAGGTTCAC

544gH1 T2

GTGGCATTAATCCCGGAAATCAGTACACTACATATAAAAGAAATCTAAAGGGCAGAGCA
ACGCTGACCGCGGACACCTCCACAAGCACTGTCTACA

544gH1 T3

AGAGAAGGCTACCGTAATTACGGAGCCTGGTCTGCCACTGGGCCAGGGTACCCTAGT
CACAGTCTCCTCAGCTTCTACAAAGGGCCAAGAAA

544 gH1 B1

GGACCAATTGCACCTCACACTGCACTCCCTGAGAATGAGTGCCAGGAACACGAGAGAG
AATCCGAAGTCCATGGTGGCGGCAAGCTTTATTG

544 gH1 B2

GATTCCCGGGATTAATGCCACCGATCCATTCCAGGCCCTGTCCCGGAGCCTGCCTGACCC
AATGAATCCAATAATTGTGAACCTGTAGCCGCTAGC

544gH1 B3

CGTAATTACCGTAGCCTCTCTAGTACAATAGTACACTGCGGTGTCCCTCGGATCTCAGAG
ATGACAGCTCCATGTAGACAGTGTGGAGG

544gH1 F1

GAATAAAAGCTTGCCGCCACC

544gH1 R1

TTTCTTGGGCCCTTGTAGAAG

FIGURE 10 CONT.

Light Chain

544 gL1 T1

GCTTCCCGGGGTGACGTTCAAGTGACCCAGAGCCCATCCAGCCTGAGCGCATCTGTAGG
AGACCGGGTCACCATCACTTAGATCC

544 gL1 T2

TATCTGCACAAACCAGGTAAAGCCCCACAATTGCTCATCTACGGAATCTCTAACAGATT
AGTGGTGTACCAAGACAGGTTACGGGTCC

544gL1 T3

AGATTTGCCACTTATTACTGTTACAAGGTACACATCAGCCGTACACATTGGTCAGGG
TACTAAAGTAGAAATCAAACGTACGGCGTGC

544gL1 B1

GAACGTACCCCCGGGAAGCAGGAATCCAGAACAAACAGAACGACCAACAGCCTAACAGG
CAACTCATGGTGGCGGCTTCGAATCATCC

544gL1 B2

CTTACCTGGTTGTGCAGATACCAAGACAAAAAGGTGTTCCCATAACTGTTGCAAGAC
TCTGACTGGATCTACAAGTGATGGTGAC

544gL1 B3

AACAGTAATAAGTGGCGAAATCTCTGGCTGGAGAGACGAGATCGTGAGGGTGAAATCA
GTACCACTCCGGAACCGCTGAACCTGTCTG

544gL1 F1

GGATGATTCGAAGCCGCCAC

544gL1 R1

GCACGCCGTACGTTGATTTC

FIGURE 11: PLASMID MAPS OF INTERMEDIATE VECTORS PCR2.1 (544GH1)

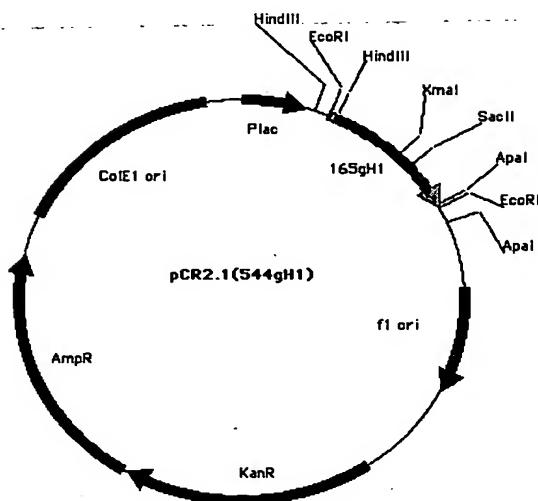


FIGURE 12: PLASMID MAPS OF INTERMEDIATE VECTORS PCR2.1 (544GL1)

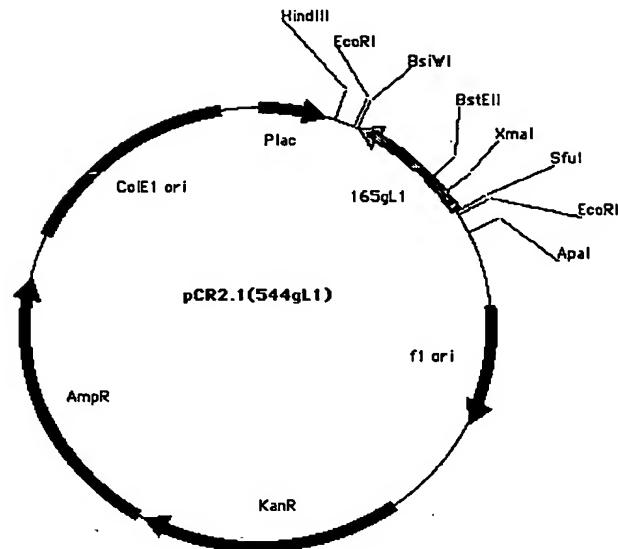


FIGURE 13: OLIGONUCLEOTIDE CASSETTES USED TO MAKE FURTHER GRAFTS**gH4**

<u>XmaI</u>	10	20	30	40	50	<u>SacII</u>
CC	GGG	AAT AAC TAC GCT ACA TAT AGG AGA AAT CTA AAG GGC AGA GCA ACG CTG ACC GC				
C	TTA TTG ATG CGA TGT ATA TCC TCT TTA GAT TTC CCG TCT CGT TGC GAC TGG					
P	G N N Y A T Y R R N L K G R A T L T A					

gH5

<u>XmaI</u>	10	20	30	40	50	<u>SacII</u>
CC	GGG	AAT AAC TAC GCT ACA TAT AGG AGA AAT CTA AAG GGC AGA GTT ACG ATG ACC GC				
C	TTA TTG ATG CGA TGT ATA TCC TCT TTA GAT TTC CCG TCT CAA TGC TAC TGG					
P	G N N Y A T Y R R K F Q G R V T M T A					

gH6

<u>XmaI</u>	10	20	30	40	50	<u>SacII</u>
CC	GGG	AAT AAC TAC GCT ACA TAT AGG AGA AAA TTC CAG GGC AGA GCA ACG CTG ACC GC				
C	TTA TTG ATG CGA TGT ATA TCC TCT TTT AAG GTC CCG TCT CGT TGC GAC TGG					
P	G N N Y A T Y R R K F Q G R A T L T A					

gH7

<u>XmaI</u>	10	20	30	40	50	<u>SacII</u>
CC	GGG	AAT AAC TAC GCT ACA TAT AGG AGA AAA TTC CAG GGC AGA GTT ACG ATG ACC GC				
C	TTA TTG ATG CGA TGT ATA TCC TCT TTT AAG GTC CCG TCT CAA TGC TAC TGG					
P	G N N Y A T Y R R K F Q G R V T M T A					

gL2

<u>XmaI</u>	10	20	30	40	50	60	<u>SacII</u>
<u>BstEII</u>	C	CGG GGT GAC GTT GTC GTG ACC CAG AGC CCA TCC AGC CTG AGC GCA TCT GTA GGA GAC CGG					
	CCA CTG CAA CAG CAC TGG GTC TCG GGT AGG TCG GAC TCG CGT AGA CAT CCT CTG GCC CAG TG						
S	R G D V V V T Q S P S S L S A S V G D R V T						

FIGURE 14: COMPETITION ASSAY, COMPETING BINDING OF FLUORESCENTLY LABELLED MOUSE 5/44 ANTIBODY WITH GRAFTED VARIANTS.

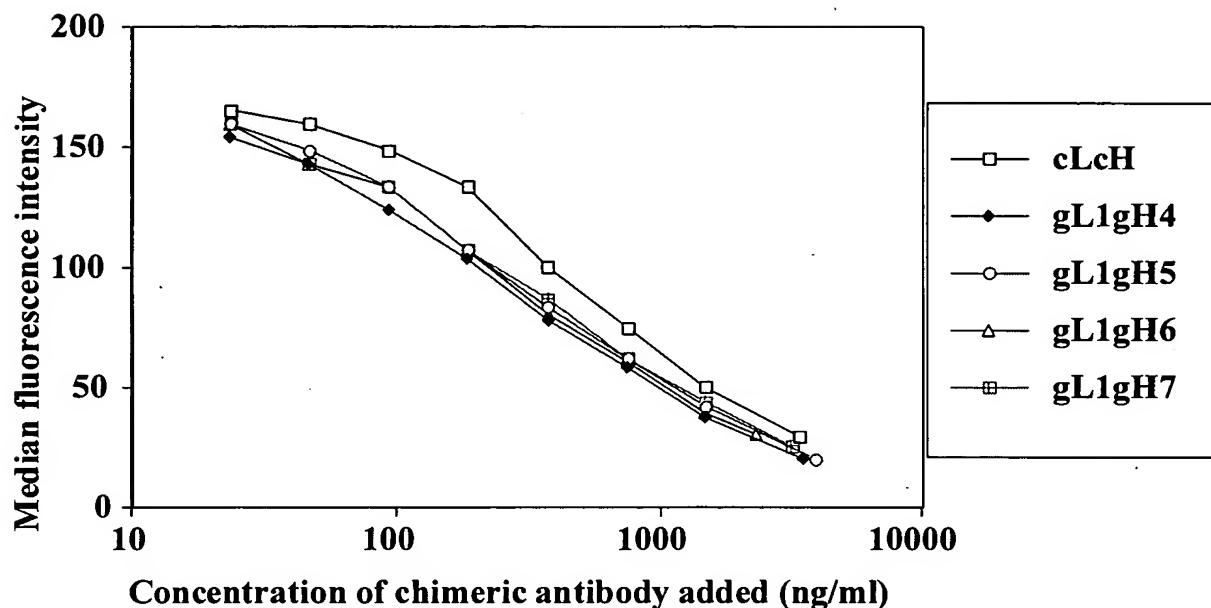


FIGURE 15: COMPETITION ASSAY, COMPETING BINDING OF FLUORESCENTLY LABELLED MOUSE 5/44 ANTIBODY WITH GRAFTED VARIANTS.

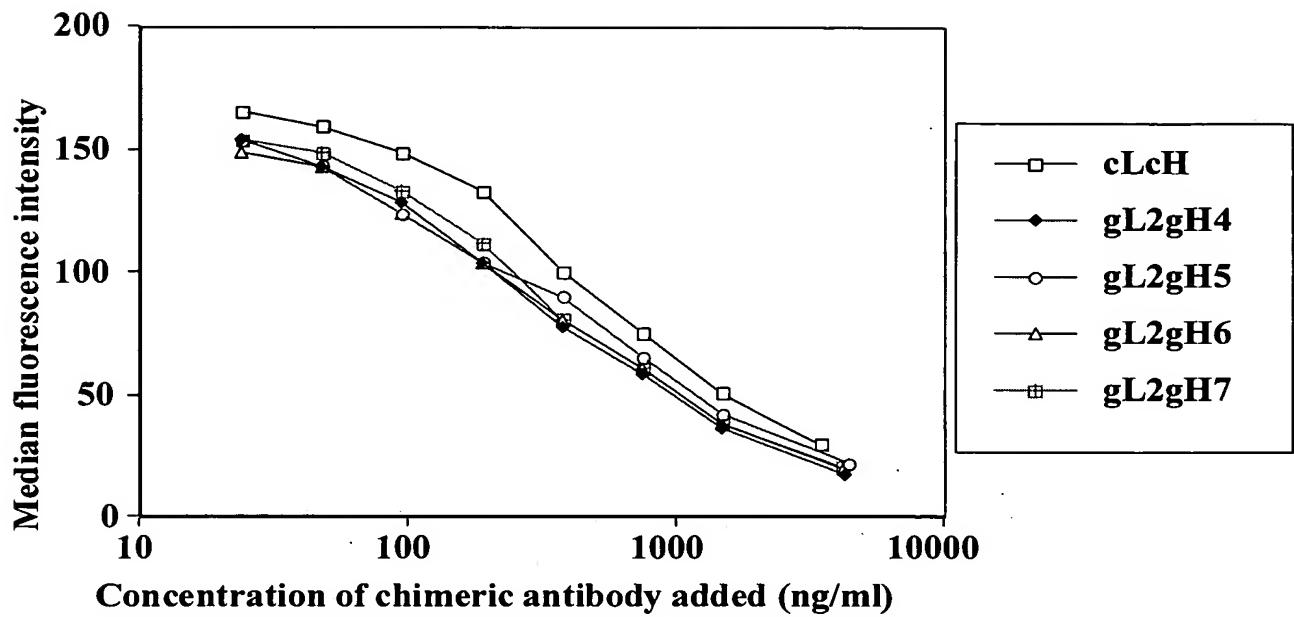


FIGURE 16: FULL DNA SEQUENCE OF GRAFTED HEAVY AND LIGHT CHAINS**a) Heavy Chain**

10	20	30	40	50	60												
AAGCTTGCCG	CCACC	ATG	GAC	TTC	GGA	TTC	TCT	CTC	GTG	TTC	CTG	GCA	CTC	ATT	CTC	AAG	
TTCGAACGGC	GGTGG	TAC	CTG	AAG	CCT	AAG	AGA	GAG	CAC	AAG	GAC	CGT	GAG	TAAG	GAG	TTC	
M	D	F	G	F	S	L	V	F	L	A	L	I	L	K	>		
70	80	90	100	110													
GGA	GTG	CAG	TGT	GAG	GTG	CAA	TTG	GTC	CAG	TCA	GGA	GCA	GAG	GTT	AAG	AAG	CCT
CCT	CAC	GTC	ACA	CTC	CAC	GTT	AAC	CAG	GTC	AGT	CCT	CGT	CTC	CAA	TTC	TTC	GGA
G	V	Q	C	E	V	Q	L	V	Q	S	G	A	E	V	K	K	CCA
120	130	140	150	160	170												
GCT	TCC	GTC	AAA	GTT	TCG	TGT	AAG	GCT	AGC	GGC	TAC	AGG	TTC	ACA	AAT	TAT	TGG
CGA	AGG	CAG	TTT	CAA	AGC	ACA	TTC	CGA	TCG	CCG	ATG	TCC	AAG	TGT	TTA	ATA	ACC
A	S	V	K	V	S	C	K	A	S	G	Y	R	F	T	N	Y	W
180	190	200	210	220	230												
CAT	TGG	GTC	AGG	CAG	GCT	CCG	GGA	CAA	GGC	CTG	GAA	TGG	ATC	GGT	GGC	ATT	AAT
GTA	ACC	CAG	TCC	GTC	CGA	GGC	CCT	GTT	CCG	GAC	CTT	ACC	TAG	CCA	CCG	TAA	TTA
H	W	V	R	Q	A	P	G	Q	G	L	E	W	I	G	G	I	N
240	250	260	270	280													
GGG	AAT	AAC	TAC	GCT	ACA	TAT	AGG	AGA	AAA	TTC	CAG	GGC	AGA	GTT	ACG	ATG	ACC
CCC	TTA	TTG	ATG	CGA	TGT	ATA	TCC	TCT	TTT	AAG	GTC	CCG	TCT	CAA	TGC	TAC	TGG
G	N	N	Y	A	T	Y	R	R	K	F	Q	G	R	V	T	M	T
290	300	310	320	330	340												
GAC	ACC	TCC	ACA	AGC	ACT	GTC	TAC	ATG	GAG	CTG	TCA	TCT	CTG	AGA	TCC	GAG	GAC
CTG	TGG	AGG	TGT	TCG	TGA	CAG	ATG	TAC	CTC	GAC	AGT	AGA	GAC	TCT	AGG	CTC	CTG
D	T	S	T	S	T	V	Y	M	E	L	S	S	L	R	S	E	D
350	360	370	380	390	400												
GCA	GTG	TAC	TAT	TGT	ACT	AGA	GAA	GGC	TAC	GGT	AAT	TAC	GGG	GCC	TGG	TTC	GCC
CGT	CAC	ATG	ATA	ACA	TGA	TCT	CTT	CCG	ATG	CCA	TTA	ATG	CCT	CGG	ACC	AAG	CGG
A	V	Y	Y	C	T	R	E	G	Y	G	N	Y	G	A	W	F	A
410	420	430	440	450													
TGG	GGC	CAG	GGT	ACC	CTA	GTC	ACA	GTC	TCC	TCA	GCT	TCT	ACA	AAG	GGC	CCA	TCC
ACC	CCG	GTC	CCA	TGG	GAT	CAG	TGT	CAG	AGG	AGT	CGA	AGA	TGT	TTC	CCG	GGT	AGG
W	G	Q	G	T	L	V	T	V	S	S	A	S	T	K	G	P	S
460	470	480	490	500	510												
TTC	CCC	CTG	GCG	CCC	TGC	TCC	AGG	AGC	ACC	TCC	GAG	AGC	ACA	GCC	GCC	CTG	GGC
AAG	GGG	GAC	CGC	GGG	ACG	AGG	TCC	TCG	TGG	AGG	CTC	TCG	TGT	CGG	CGG	GAC	ACG
F	P	L	A	P	C	S	R	S	T	S	E	S	T	A	A	L	G
520	530	540	550	560	570												
CTG	GTC	AAG	GAC	TAC	TTC	CCC	GAA	CCG	GTG	ACG	GTG	TCG	TGG	AAC	TCA	GGC	GCC
GAC	CAG	TTC	CTG	ATG	AAG	GGG	CTT	GGC	CAC	TGC	CAC	AGC	ACC	TTG	AGT	CCG	CTG
L	V	K	D	Y	F	P	E	P	V	T	V	S	W	N	S	G	A
580	590	600	610	620	630												
ACC	AGC	GGC	GTG	CAC	ACC	TTC	CCG	GCT	GTC	CTA	CAG	TCC	TCA	GGA	CTC	TAC	TCC
TGG	TCG	CCG	CAC	GTG	TGG	AAG	GGC	CGA	CAG	GAT	GTC	AGG	AGT	CCT	GAG	ATG	AGG
T	S	G	V	H	T	F	P	A	V	L	Q	S	S	G	L	Y	S
																	L>

FIGURE 16 CONT.

640 650 660 670 680
 AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAG ACC TAC ACC TGC AAC
 TCG TCG CAC CAC TGG CAC GGG AGG TCG TCG AAC CCG TGC TTC TGG ATG TGG ACG TTG
 S S V V T V P S S S L G T K T Y T C N>

 690 700 710 720 730 740
 GTA GAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AGA GTT G GTGAGAGGCC
 CAT CTA GTG TTC GGG TCG TTG TGG TTC CAC CTG TTC TCT CAA C CACTCTCCGG
 V D H K P S N T K V D K R V>

 750 760 770 780 790 800 810
 AGCACAGGGGA GGGAGGGTGT CTGCTGGAAG CCAGGCTCAG CCCTCCTGCC TGGACGCACC CGGGCTGTGC
 TCGTGTCCCT CCCTCCCACA GACGACCTTC GGTCCGAGTC GGGAGGACGG ACCTGCGTGG GGCGACACCG

 820 830 840 850 860 870 880
 AGCCCCCAGCC CAGGGCAGCA AGGCATGCC CATCTGTCTC CTCACCCGGA GGCCTCTGAC CACCCCCACTC
 TCAGGGGTCGG GTCCCGTCGT TCCGTACGGG TAGACAGAG GAGTGGGCCT CCGGAGACTG GTGGGGTGAG

 890 900 910 920 930 940 950
 ATGCCCCAGGG AGAGGGTCTT CTGGATTTT CCACCAGGCT CGGGGCAGCC ACAGGGCTGGA TGCCCCCTAAC
 TACGGGGTCCC TCTCCCCAGAA GACCTAAAAA GGTGGTCCGA GGCCCCTCGG TGTCCGACCT ACGGGGATGG

 960 970 980 990 1000 1010 1020
 CCAGGCCCTG CGCATACAGG GGCAGGTGCT GCGCTCAGAC CTGCCAAGAG CCATATCCGG GAGGACCCCTG
 GGTCCGGGAC GCGTATGTCC CCGTCCACGA CGCGAGTCTG GACGGTTCTC GGTATAAGGCC CTCCCTGGGAC

 1030 1040 1050 1060 1070 1080 1090
 CCCCTGACCT AAGCCCACCC CAAAGGCCAA ACTCTCCACT CCCTCAGCTC AGACACCTTC TCTCCTCCCA
 GGGGACTGGA TTGGGGTGGG GTTTCCGGTT TGAGAGGTGA GGGAGTCGAG TCTGTGGAAG AGAGGAGGGT

 1100 1110 1120 1130 1140 1150
 GATCTGAGTA ACTCCCAATC TTCTCTCTGC A GAG TCC AAA TAT GGT CCC CCA TGC CCA CCA
 CTAGACTCAT TGAGGGTTAG AAGAGAGACG T CTC AGG TTT ATA CCA GGG GGT ACG GGT GGT
 E S K Y G P P C P P>

 1160 1170 1180 1190 1200 1210 1220
 TGC CCA GGT AAGCCAACCC AGGCCTCGCC CTCCAGCTCA AGGCAGGACA GGTGCCCTAG AGTAGCCTGC
 ACG GGT CCA TTGGGTTGGG TCCGGAGCGG GAGGTCGAGT TCCGCCCTGT CCACGGGATC TCATCGGACG
 C P>

 1230 1240 1250 1260 1270 1280
 ATCCAGGGGAC AGGGCCCAGC CGGGTGCTGA CGCATCCACC TCCATCTCTT CCTCA GCA CCT GAG TTC
 TAGGTCCCTG TCCGGGGTCG GCCCACGACT GCGTAGGTGG AGGTAGAGAA GGAGT CGT GGA CTC AAG
 A P E F>

 1290 1300 1310 1320 1330 1340
 CTG GGG GGA CCA TCA GTC TTC CTG CCC CCA AAA CCC AAG GAC ACT CTC ATG ATC
 GAC CCC CCT GGT AGT CAG AAG GAC AAG GGG GGT TTT GGG TTC CTG TGA GAG TAC TAG
 L G G P S V F L F P P K P K D T L M I>

 1350 1360 1370 1380 1390 1400
 TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG
 AGG GCC TGG GGA CTC CAG TGC ACG CAC CAC CAC CTG CAC TCG GTC CTT CTG GGG CTC
 S R T P E V T C V V V D V S Q E D P E>

FIGURE 16 CONT.

1410 1420 1430 1440 1450
 GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG
 CAG GTC AAG TTG ACC ATG CAC CTA CCG CAC CTC CAC GTC TTA CGG TTC TGT TTC GGC
 V Q F N W Y V D G V E V H N A K T K P>

 1460 1470 1480 1490 1500 1510
 CGG GAG GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC
 GCC CTC CTC GTC AAG TTG TCG TGC ATG GCA CAC CAG TCG CAG GAG TGG CAG GAC GTG
 R E E Q F N S T Y R V V S V L T V L H>

 1520 1530 1540 1550 1560 1570
 CAG GAC TGG CTG AAC GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CCC
 GTC CTG ACC GAC TTG CCG TTC CTC ATG TTC ACN CAG AGG TTG TTT CCG GAG GGC
 Q D W L N G K E Y K C K V S N K G L P>

 1580 1590 1600 1610 1620 1630
 TCC TCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGTGG GACCCACGGG GTGCGAGGGC
 AGG AGG TAG CTC TTT TGG TAG AGG TTT CGG TTT CCACC CTGGGTGCC CACGCTCCCG
 S S I E K T I S K A K>

 1640 1650 1660 1670 1680 1690 1700
 CACATGGACA GAGGTCAAGCT CGGGCCCACCC TCTGCCCTGG GAGTGACCGC TGTGCCAACCT CTCGTCCCTA
 GTGTACCTGT CTCCAGTCGA GCCGGGTGGG AGACGGGACC CTCACTGGCG ACACGGTTGG AGACAGGGAT

 1710 1720 1730 1740 1750
 CA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG GAG ATG
 GT CCC GTC GGG GCT CTC GGT GTC CAC ATG TGG GAC GGG GGT AGG GTC CTC CTC TAC
 G Q P R E P Q V Y T L P P S Q E E M>

 1760 1770 1780 1790 1800 1810
 ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC
 TGG TTC TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT CCG AAG ATG GGG TCG CTG TAG
 T K N Q V S L T C L V K G F Y P S D I>

 1820 1830 1840 1850 1860 1870
 GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC
 CGG CAC CTC ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA GGG
 A V E W E S N G Q P E N N Y K T T P P>

 1880 1890 1900 1910 1920
 GTG CTG GAC TCC GAC GGC TCC TTC TCC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC
 CAC GAC CTG AGG CTG CCG AGG AAG AAG GAG ATG TCG TCC GAT TGG CAC CTG TTC TCG
 V L D S D G S F F L Y S R L T V D K S>

 1930 1940 1950 1960 1970 1980
 AGG TGG CAG GAG GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC
 TCC ACC GTC CTC CCC TTA CAG AAG AGT ACG AGG CAC TAC GTA CTC CGA GAC GTG TTG
 R W Q E G N V F S C S V M H E A L H N>

 1990 2000 2010 2020 2030 2040
 CAC TAC ACA CAG AAG AGC CTC TCC CTG TCT CTG GGT AAA TGA GTGC CAGGGCCGGC
 GTG ATG TGT GTC TTC TCG GAG AGG GAC AGA GAC CCA TTT ACT CACCG GTCCCCGGCCG
 H Y T Q K S L S L S L G K *>

 2050 2060 2070 2080 2090 2100 2110
 AAGCCCCCGC TCCCCGGGCT CTCGGGGTCG CGCGAGGATG CTTGGCACGT ACCCCGTCTA CATACTTCCC
 TTCGGGGGCG AGGGGCCCGA GAGCCCCAGC GCGCTCCTAC GAACCGTGCA TGGGGCAGAT GTATGAAGGG

FIGURE 16 CONT

2120 2130 2140 2150 2160
AGGCACCCAG CATGGAAATA AAGCACCCAC CACTGCCCTG GCTCGAATTG
TCCGTGGTC GTACCTTAT TTCTGGGTG GTGACGGGAC CGAGCTTAAG

FIGURE 16 CONT.**b) Light Chain**

10 20 30 40 50 60
TTCGAAGCCG CCACC ATG AAG TTG CCT GTT AGG CTG TTG GTG CTT CTG TTG TTC TGG ATT
AAGCTTCGGC GGTGG TAC TTC AAC GGA CAA TCC GAC AAC CAC GAA GAC AAC AAG ACC ACC TAA
M K L P V R L L V L L L F W I>

70 80 90 100 110
CCT GCT TCC CGG GGT GAC GTT CAA GTG ACC CAG AGC CCA TCC AGC CTG AGC GCA TCT
GGA CGA AGG GCC CCA CTG CAA GTT CAC TGG GTC TCG GGT AGG TCG GAC TCG CGT AGA
P A S R G D V Q V T Q S P S S L S A S>

120 130 140 150 160 170
GTA GGA GAC CGG GTC ACC ATC ACT TGT AGA TCC AGT CAG AGT CTT GCA AAC AGT TAT
CAT CCT CTG GCC CAG TGG TAG TGA ACA TCT AGG TCA GTC TCA GAA CGT TTG TCA ATA
V G D R V T I T C R S S Q S L A N S Y>

180 190 200 210 220 230
GGG AAC ACC TTT TTG TCT TGG TAT CTG CAC AAA CCA GGT AAA GCC CCA CAA TTG CTC
CCC TTG TGG AAA AAC AGA ACC ATA GAC GTG TTT GGT CCA TTT CGG GGT GTT AAC GAG
G N T F L S W Y L H K P G K A P Q L L>

240 250 260 270 280
ATC TAC GGA ATC TCT AAC AGA TTT AGT GGT GTA CCA GAC AGG TTC AGC GGT TCC GGA
TAG ATG CCT TAG AGA TTG TCT AAA TCA CCA CAT GGT CTG TCC AAG TCG CCA AGG CCT
I Y G I S N R F S G V P D R F S G S G>

290 300 310 320 330 340
AGT GGT ACT GAT TTC ACC CTC ACG ATC TCG TCT CTC CAG CCA GAA GAT TTC GCC ACT
TCA CCA TGA CTA AAG TGG GAG TGC TAG AGC AGA GAG GTC GGT CTT CTA AAG CGG TGA
S G T D F T L T I S S L Q P E D F A T>

350 360 370 380 390 400
TAT TAC TGT TTA CAA GGT ACA CAT CAG CCG TAC ACA TTC GGT CAG GGT ACT AAA GTA
ATA ATG ACA AAT GTT CCA TGT GTA GTC GGC ATG TGT AAG CCA GTC CCA TGA TTT CAT
Y Y C L Q G T H Q P Y T F G Q G T K V>

410 420 430 440 450
GAA ATC AAA CGT ACG GTA GCG GCC CCA TCT GTC TTC ATC TTC CCG CCA TCT GAT GAG
CTT TAG TTT GCA TGC CAT CGC CGG GGT AGA CAG AAG TAG AAG GGC GGT AGA CTA CTC
E I K R T V A A P S V F I F P P S D E>

460 470 480 490 500 510
CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC TTC TAT CCC AGA
GTC AAC TTT AGA CCT TGA CGG AGA CAA CAC ACG GAC GAC TTA TTG AAG ATA GGG TCT
Q L K S G T A S V V C L L N N F Y P R>

520 530 540 550 560 570
GAG GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC TCC CAG GAG
CTC CGG TTT CAT GTC ACC TTC CAC CTA TTG CGG GAG GTT AGC CCA TTG AGG GTC CTC
E A K V Q W K V D N A L Q S G N S Q E>

580 590 600 610 620 630
AGT GTC ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC AGC CTC AGC AGC ACC CTG ACG
TCA CAG TGT CTC GTC CTG TCG TTC CTG TCG TGG ATG TCG GAG TCG TCG TGG GAC TGC
S V T E Q D S K D S T Y S L S S T L T>

640 650 660 670 680

FIGURE 16 CONT

CTG AGC AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT CAG
GAC TCG TTT CGT CTG ATG CTC TTT GTG TTT CAG ATG CGG ACG CTT CAG TGG GTA GTC
L S K A D Y E K H K V Y A C E V T H Q>
690 700 710 720 730 740
GGC CTG AGC TCG CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG TGT TAG AGGGA
CCG GAC TCG AGC GGG CAG TGT TTC TCG AAG TTG TCC CCT CTC ACA ATC TCCCT
G L S S P V T K S F N R G E C *>
750 760 770 780
GAAGTGCCCC CACCTGCTCC TCAGTTCCAG CCTGGGAATT C
CTTCACGGGG GTGGACGAGG AGTCAAGGTC GGACCCTTAA G

FIGURE 17: STRUCTURE OF AN ANTIBODY-NAC-GAMMA CALICHEAMICIN DMH CONJUGATE

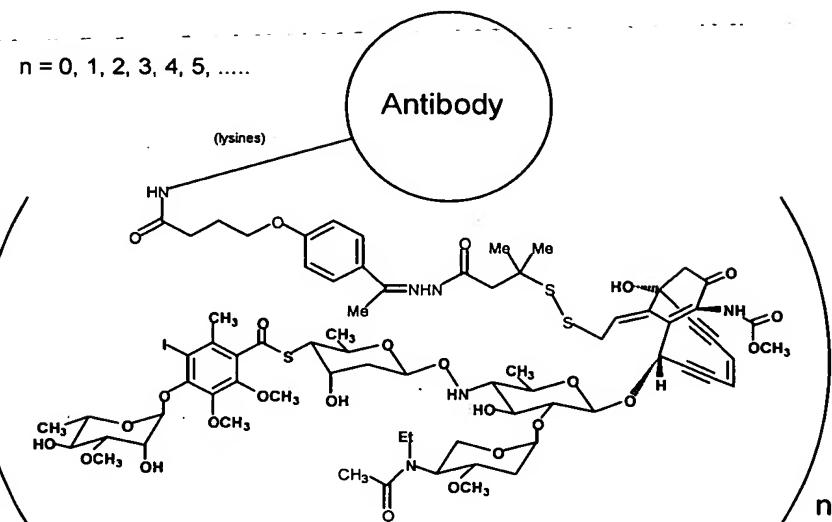


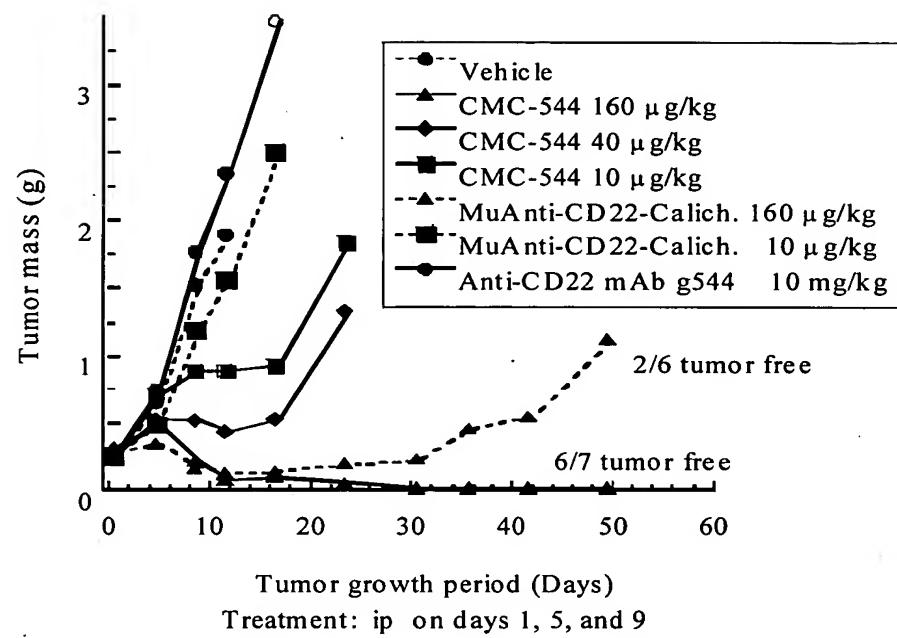
FIGURE 18: EFFECT OF CMC-544 ON GROWTH OF RAMOS B-CELL LYMPHOMA

FIGURE 19: EFFECT OF CMC-544 ON LARGE B-CELL LYMPHOMAS

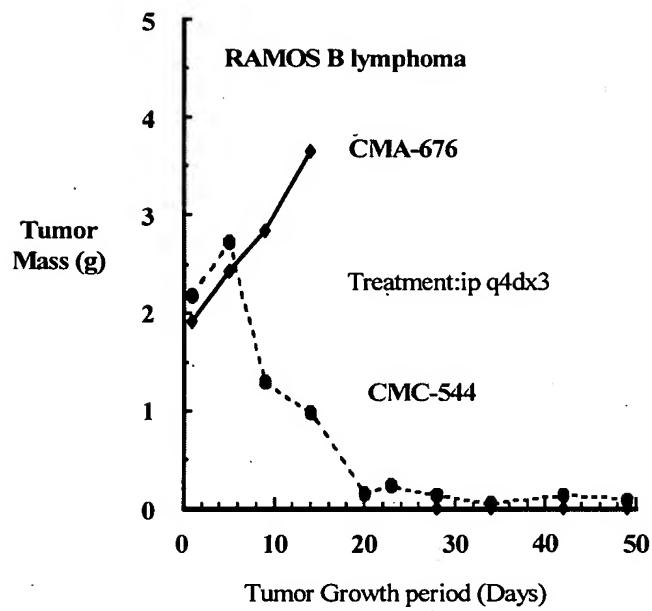


FIGURE 20: EFFECT OF CMC-544 MADE WITH THE CMA AND CMC CONJUGATION PROCEDURES ON THE GROWTH OF RL LYMPHOMA

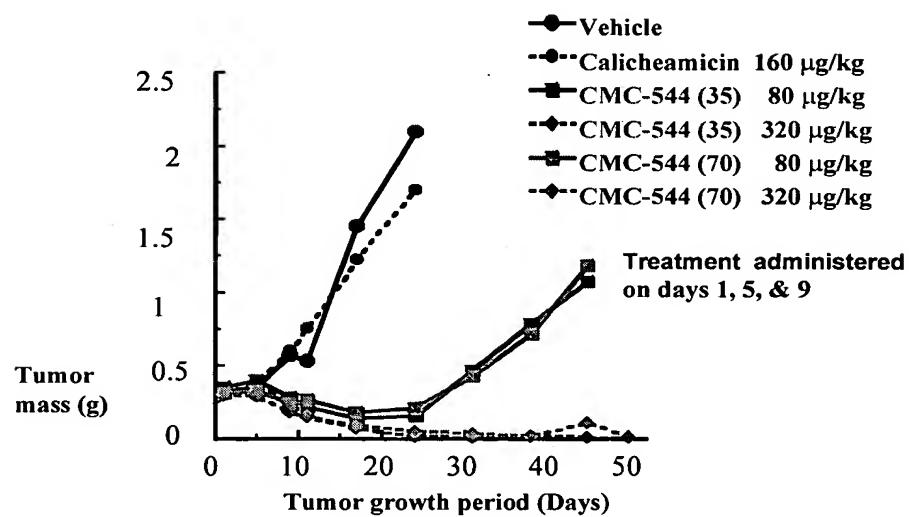


FIGURE 21: RITUXIMAB (RITUXAN™)-TREATED LARGE RL LYMPHOMA IS SUSCEPTIBLE TO CMC-544

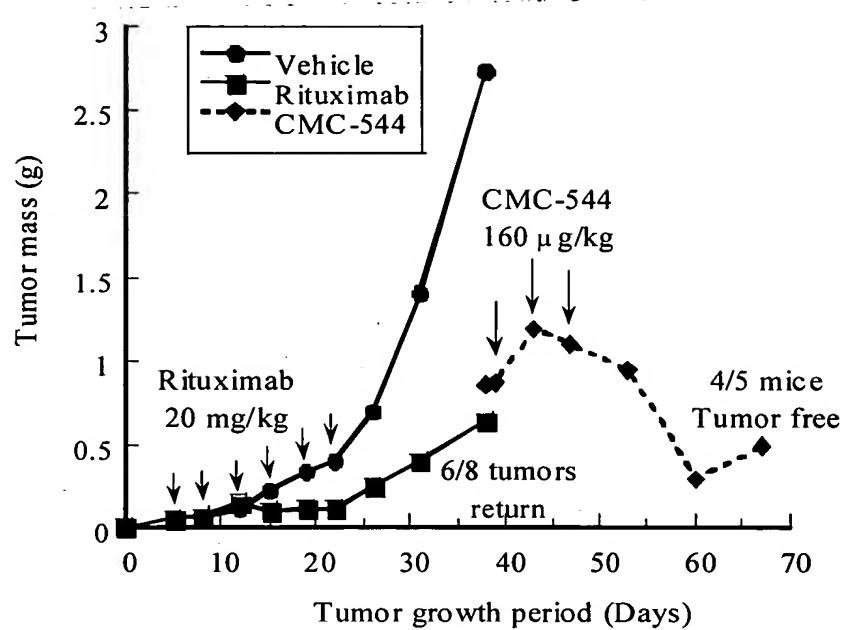


FIGURE 22: EFFECT OF RITUXIMAB (RITUXAN™) ON THE CYTOTOXIC ACTIVITY OF CMC-544

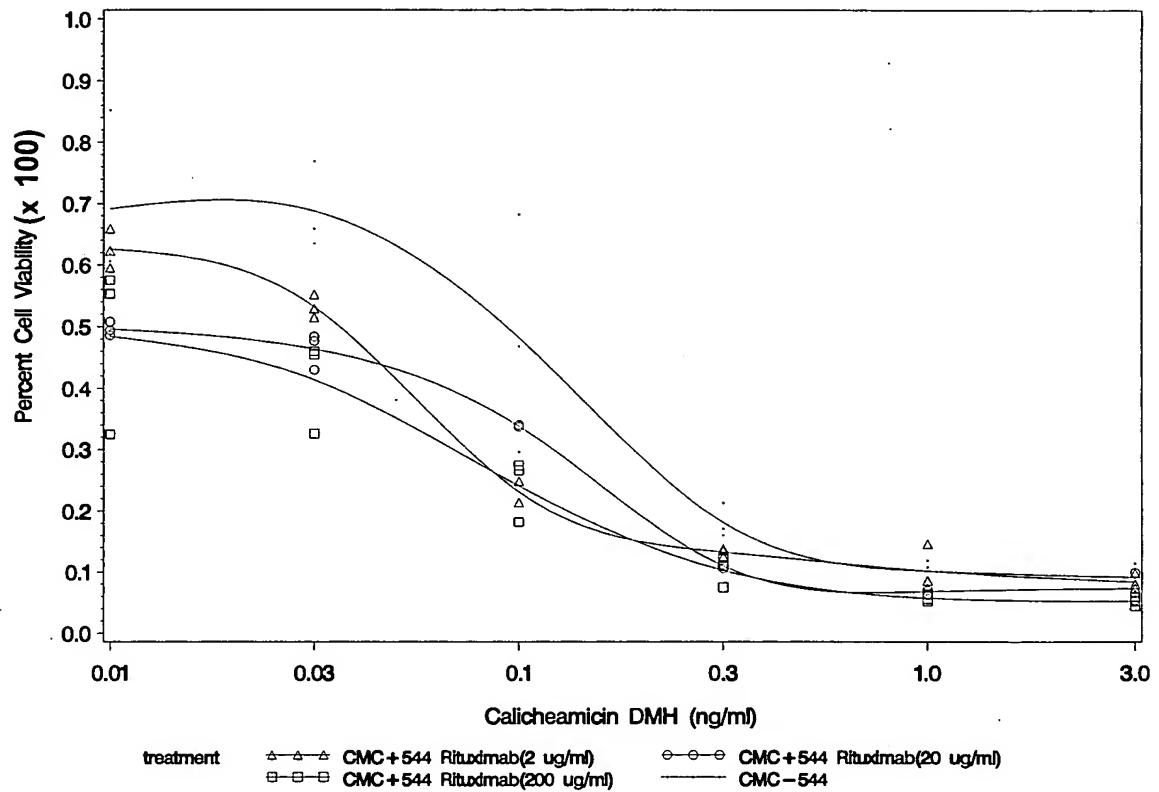


FIGURE 23: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™)-, AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED EARLY RAMOS B LYMPHOMA

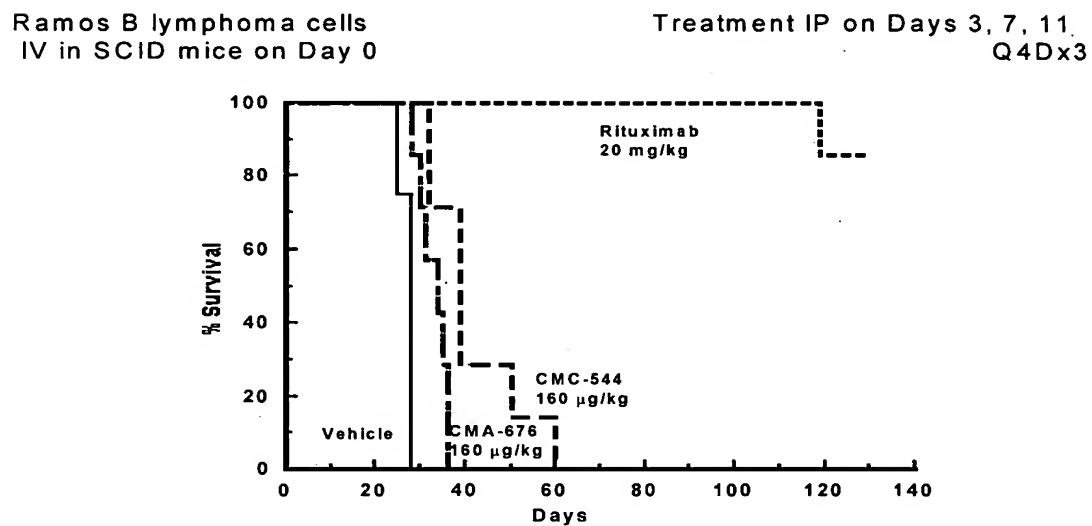


FIGURE 24: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

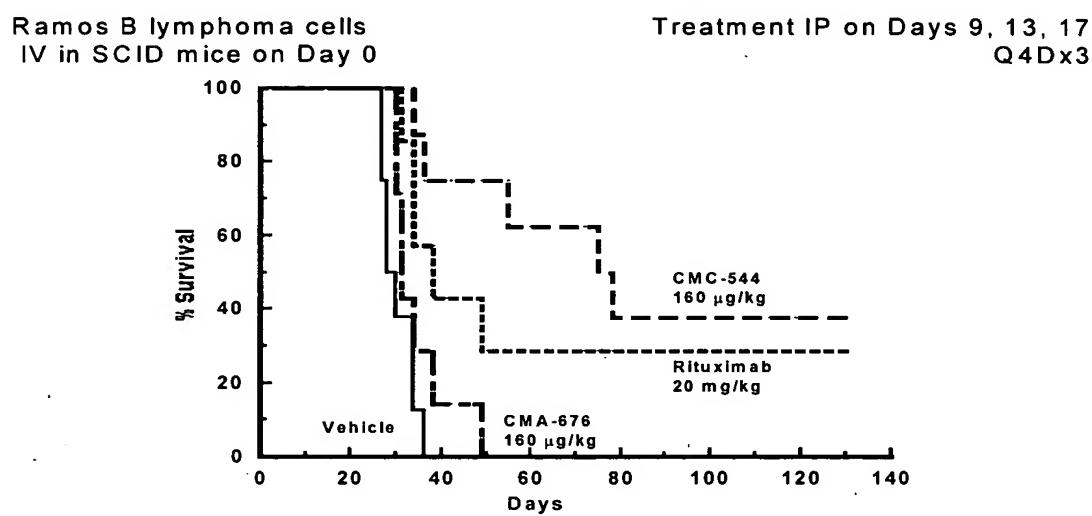


FIGURE 25: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

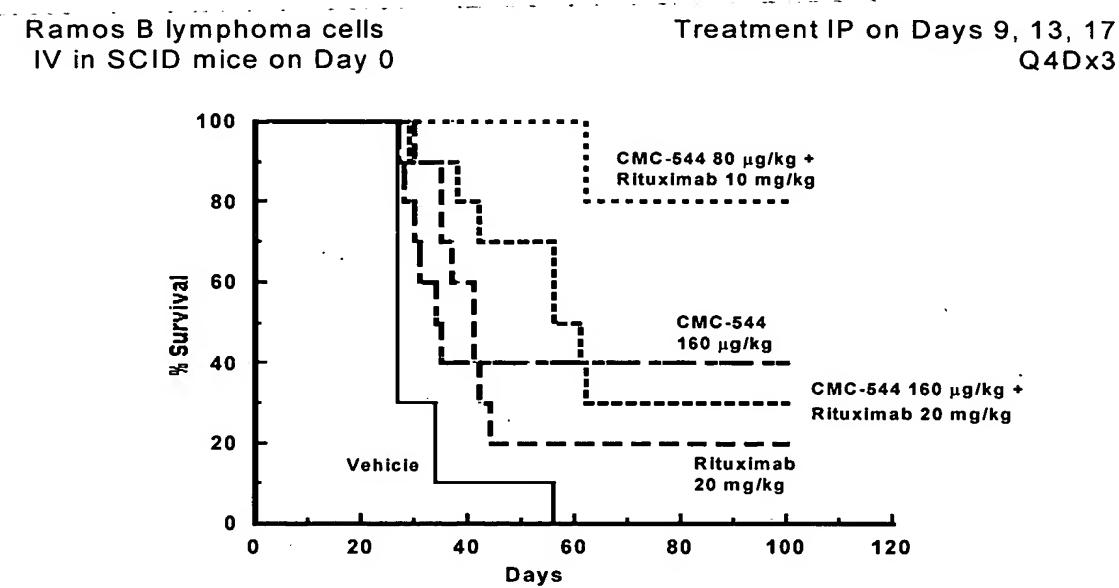


FIGURE 26: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

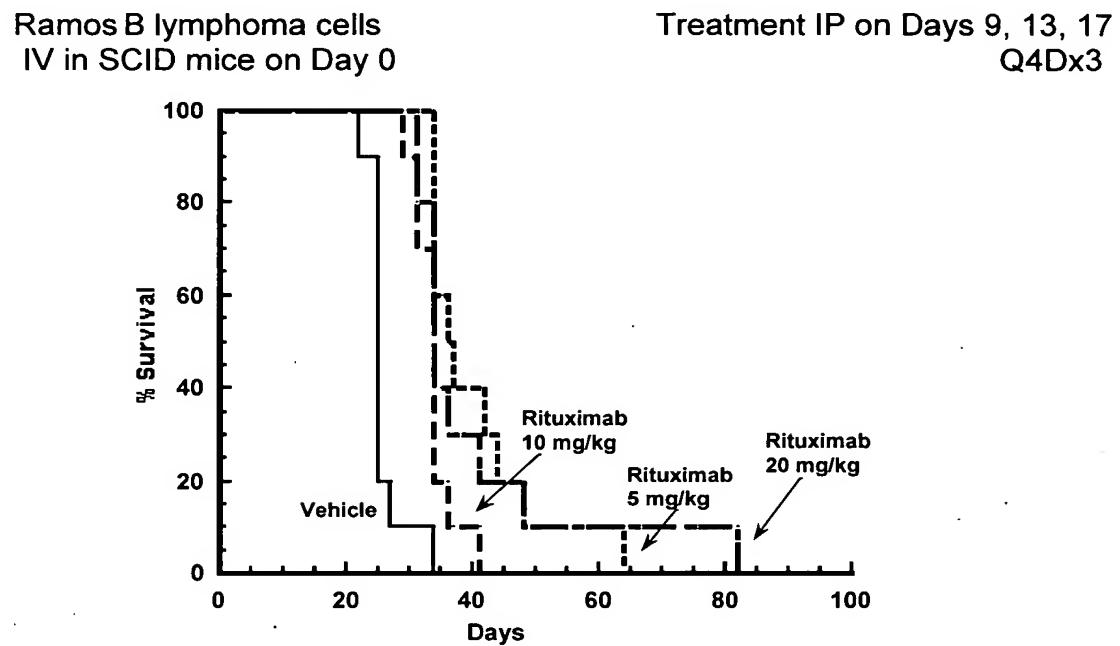


FIGURE 27: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

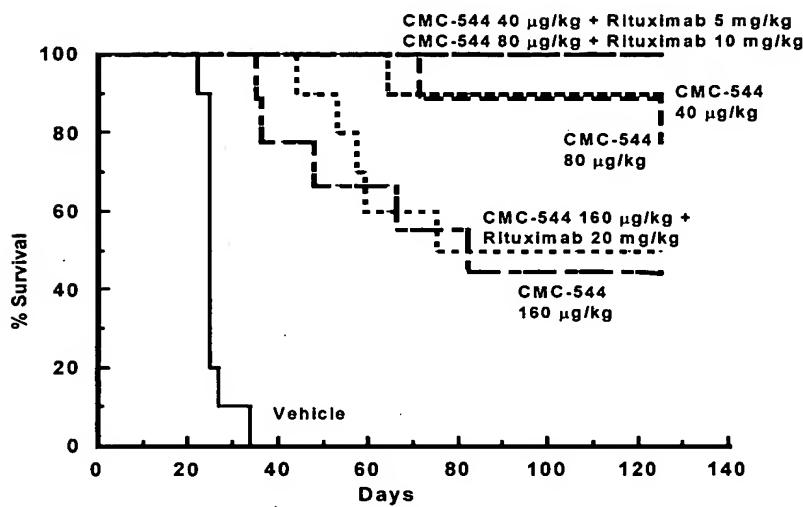


FIGURE 28: ANTI-TUMOR ACTIVITY OF CMC-544 WITH/WITHOUT RITUXIMAB (RITUXAN™) ON RL NON-HODGKINS LYMPHOMA

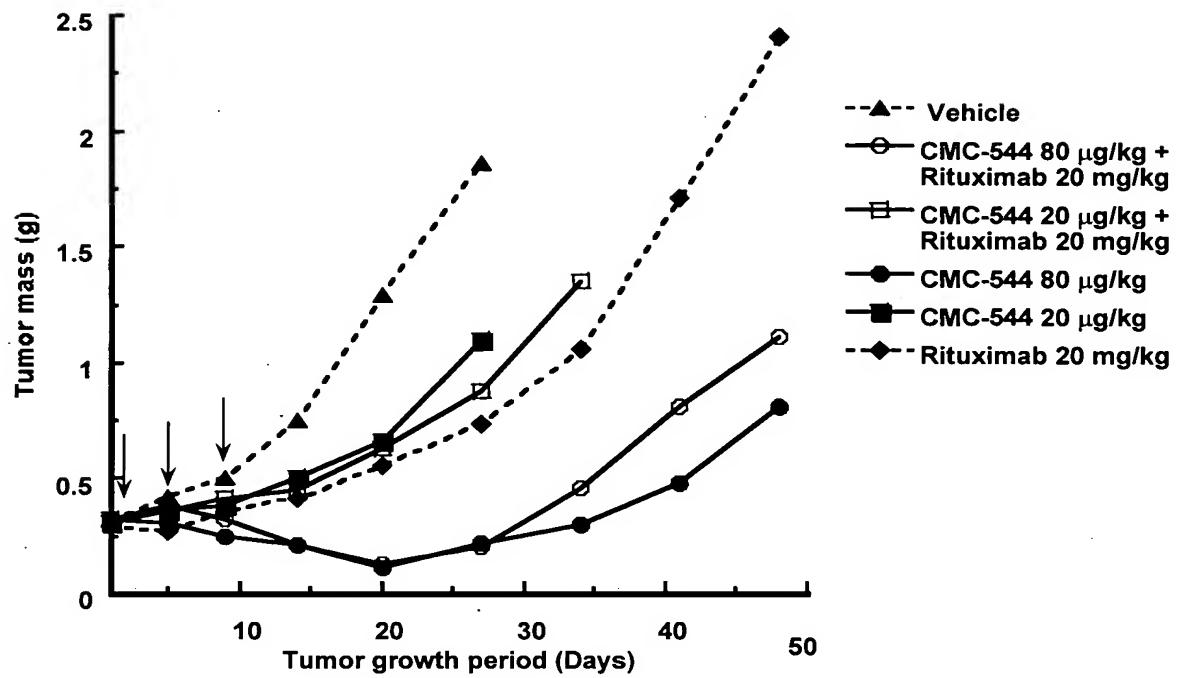


FIGURE 29: ANTI-TUMOR ACTIVITY OF CMC-544 AND CHOP ON RL NON-HODGKINS LYMPHOMA

